



N 09/524,454

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Kristian Berg et al.

Examiner: Gerald Ewoldt

Serial No.: 09/524,454

Group Art Unit: 1644

Filed: March 10, 2000

Docket No.: 697.013US1

Title: METHOD OF VACCINATION

**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

Mail Stop AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

The applicant requests review of the final rejection in the above-identified application. This request is being filed with a Notice of Appeal. Reasons for this Request are provided starting on page 5.

No amendments to application or claims are being made at this time.

This Request is accompanied by a Petition, as well as the appropriate fee, to obtain a three-month extension of the period for responding to the Office Action, thereby moving the deadline for response from February 29, 2006 to May 29, 2006.

***§112 Rejections of the Claims***

**Enablement**

Claims 2, 4, 6, 8-10 and 22 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner alleges that the specification provides insufficient evidence that the claimed method could be used for expressing a molecule on a cell for the following reasons.

- (a) The Examiner asserts that only certain antigen presenting cells are capable of presenting antigens and generating an immune response. In response, Applicant submits that all cells are able to generate an immune response through presentation by major histocompatibility (MHC) molecules that are possessed by essentially all cells.
- (b) The Examiner asserts that the specification exemplifies use of only two photosensitizers. Applicant submits that while two photosensitizers were used successfully to achieve release of antigenic molecules into the cytosol (see Examples), the specification describes many others that may be used and evidence has been provided of the use of other photosensitizers

to achieve release of antigenic molecules into the cytosol (see March 23, 2004 Response). Once released into the cytosol, such antigenic molecules are processed and presented on the cell surface for immune presentation (see, e.g., Example 2).

- (c) The Examiner asserts that the specification does not show cell surface expression of any molecule and that Example 3 shows the opposite. Applicant submits that Example 3 shows photochemical internalization of horseradish peroxidase (HRP) from the cell surface to the cytosol, as detected by HRP activity in the cytosol. Because HRP activity was used for detection, presentation of HRP peptides on the cell surface was not observed because these peptides were too small to possess enzymatic activity. Example 2 shows that a MART-1 peptide is internalized and presented by MHC molecules on the cell surface, as detected by cytotoxic T cells that were specific for the MART-1 peptide. Thus, the specification clearly does provide evidence not only of cell surface expression (via MHC machinery) but also of an immune response (cytotoxic T cell reaction against the surface-displayed MART-1 peptide).

Applicant submits that the specification fully enables the claims and request withdrawal of this rejection.

### Written Description

Claims 2, 4, 6, 8-10 and 22 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Examiner alleges that Applicant was not in possession of “a molecule comprising an antigenic peptide” and “lysomotropic weak base thereof.”

Applicant submits that the phrase “a lysomotropic weak base” is a well-understood term of art that has been used widely in scientific publications for at least twenty-three years. See, for example, Helenius, A. et al., *J. Gen Virol.* **1982**, *58 Pt.1*, 47-61; Styrt, B., et al., *Blood* **1986**, 67, 334-42; Zdolsek, J.M. et al., *Photochem. Photobiol.* **1990**, *51*, 67-76; and Antunes, F. et al., *Biochem. J.* **2001**, 356, 549-555 (copies previously provided to the Examiner). Applicant further submits that “a molecule comprising an antigenic peptide” is fully supported by the application as filed, for example, at page 4, lines 35-37, and in the Examples.

However, while Applicant asserts that those skilled in the art clearly would understand that the inventors were in possession of the invention as of the filing date of the application and

requests withdrawal of this rejection, Applicant would amend the claims to obviate this rejection if it would place the application in condition for allowance.

### ***§102 Rejection of the Claims***

Claims 2, 4, 6, 8-10 and 22 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by PCT Application Publication No. WO96/07432 by Berg. The Examiner alleges that WO96/07432 inherently discloses a method of expressing an antigenic molecule on the surface of a viable cancer cell.

Applicant submits that WO96/07432 does not teach antigen presentation or stimulation of an immune response either explicitly or implicitly, and that the methods provided by WO96/07432 are not performed in a way that lead to antigen presentation and/or stimulation of an immune response. In particular, WO96/07432 discloses methods that lead to cell death (where no antigen presentation can occur and hence an immune response cannot be stimulated) and/or to transfer of genetic material (no display of an antigen and no immune response).

Applicant further submits that anticipation rejection based on inherency must be supported by factual and technical grounds establishing that the inherent feature must flow as a necessary conclusion, not simply a possible conclusion, from the teaching of the cited art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Int. 1990); *In re Oelrich*, 666 F.2d 578, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981). Here, there are factual and technical grounds establishing that the methods of WO96/07432 would NOT lead to cell surface expression and/or immune stimulation because the cells are killed by the WO96/07432 methods or no antigenic molecule is used.

Applicant requests withdrawal of this rejection.

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Conclusion

The applicant respectfully submits that all of the pending claims are in condition for allowance, and such action is earnestly solicited. The Patent Office is invited to telephone the below-signed attorney at (516) 795-6820 to discuss any questions which may remain with respect to the present application.

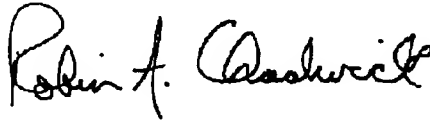
If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

KRISTIAN BERG ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.  
P.O. Box 2938  
Minneapolis, MN 55402  
(516) 795-6820

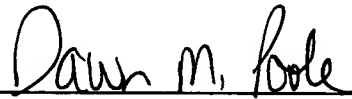


Date May 26, 2006 By \_\_\_\_\_  
Robin A. Chadwick  
Reg. No. 36,477

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 26 day of May, 2006.

Dawn M. Poole

Name



Signature